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Michelle Hobson

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

WANG and PABO

For: **DIMERIZING PEPTIDES**

Serial No.: 09/636,243

Filed: August 10, 2000

Atty. Docket No.: 8325-1004 (M4-US1)

Examiner: T. Wessendorf

Group Art Unit: 1639

Confirmation No.: 6438

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Reply Brief is filed in response to an Examiner's Answer mailed December 23, 2009, making a Reply Brief due on or before February 23, 2010. Accordingly, this Reply Brief is timely filed.

REAL PARTIES IN INTEREST

The Massachusetts Institute of Technology, the assignee of record of the above-referenced patent application by virtue of an assignment recorded on April 2, 2001 at Reel 011676, Frame 0049. Sangamo BioSciences, Inc., is the exclusive licensee of the above-referenced patent application. Thus, the Massachusetts Institute of Technology and Sangamo BioSciences, Inc. are the real parties in interest in this matter.

RELATED APPEALS AND INTERFERENCES

Appellants note that this case was previously appealed. The Board decision reversing the previous rejections and setting forth new grounds of rejection was mailed on May 30, 2007 and was attached to the Appeal Brief.

STATUS OF THE CLAIMS

Pending: claims 5, 6, 20 and 21

Canceled: claims 1-4 and 7-19

Rejected: claims 5, 6, 20 and 21

Appealed: claims 5, 6, 20 and 21

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Whether claims 5, 6, 20 and 21 are unpatentable under 35 U.S.C. § 103(a) as obvious over Pomerantz (1998) *Biochemistry* 37(4):965-970 (hereinafter “Pomerantz”) in view of Krylov et al. (1994) *EMBO J.* 13(12):2849-2861 (hereinafter “Krylov”).

ARGUMENTS

A. The claims are non-obvious over the cited references

Claims 5, 6, 20, and 21 remain rejected as allegedly obvious over Pomerantz and Krylov. (Examiner’s Answer, page 3-6). Pomerantz was cited for allegedly disclosing a zinc finger protein fused to a naturally occurring dimerization domain extracted from the

GAL4 protein and for suggesting the use of non-naturally occurring dimerization domains. *Id.* Krylov, reference 20 of Pomerantz, was cited for allegedly demonstrating that non-naturally occurring peptide linkers could be utilized to complex zinc finger proteins. *Id.*

In response to Appellants' arguments that there is no combination of the references that teaches the claimed complexes, namely complexes in which zinc finger proteins are joined to each other by non-naturally occurring peptide linkers of less than 30 amino acids, it was again asserted that Pomerantz teaches a **portion** of the full-length dimerization domain constituting a "short" peptide linker and Figure 1B of Krylov teaches coiled coil heptads of 24 amino acids in length. (Examiner's Answer, pages 6-10).

In addition, in response to Appellants' arguments that, whatever the length of Pomerantz's or Krylov's linkers, the linkers of the references are not non-naturally occurring peptides, the Examiner asserted that Pomerantz's and Krylov's linkers were "derived" from naturally occurring sequences so were somehow not naturally occurring (Examiner's Answer, page 11, emphasis in original):

In reply, both the dimers of Pomerantz and Krylov are derived peptides. Each is a short length peptide which therefore lacks significant sequence identity with a naturally occurring peptides, as read in the light of the above-cited definition in the specification. The art also defines non-naturally occurring as a recombinantly/synthetically made peptide or mutants as the ones created or taught by Krylov. These mutants are therefore non-naturally occurring as these lack significant sequence identity with the natural leucine zipper peptide, consistent with the definition in the specification.

Finally, in response to Appellants' arguments that a *prima facie* case of obviousness has not been (and cannot be) established because the proposed modifications to the references are not predictable uses of these domains, the Examiner asserted that Pomerantz suggests modifying the leucine zipper proteins of Krylov to non-naturally occurring linkers. (Examiner's Answer, pages 11-12). It was again asserted there is nothing "new, unobvious, or unpredictable in varying the length of a known dimerization domain when its sequence is known and is varied in the context it is used." (Examiner's Answer, page 12).

Appellants address the errors in the Examiner's assertions in turn.

1. The references do not teach or suggest the claimed elements

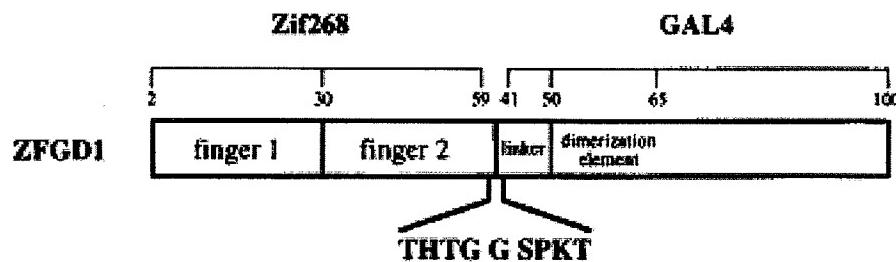
In order to establish obviousness of a claimed invention, all the features of the claims must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Thus, in the case on appeal, Pomerantz and Krylov must teach or suggest a complex comprising two fusion proteins in which each fusion protein comprises a zinc finger protein and a 30 amino acid or less non-naturally occurring peptide linker that forms a dimer with the corresponding non-naturally occurring peptide linker on a separate fusion protein. In addition, each zinc finger protein must bind to DNA in a sequence-specific manner.

For the reasons of record, there is no combination of the cited references that teaches or suggests the claimed elements.

a. Pomerantz and Krylov do not teach linkers under 30 amino acids in length

As noted, the Examiner erroneously insists that Pomerantz discloses a "portion" of the GAL-4 dimerization domain less than 30 amino acids in length. (Examiner's Answer, pages 6-10). Various parts of Pomerantz are cited in this regard, including Figure 1 and the text describing this Figure. (Examiner's Answer, pages 6-7).

The first error in the Examiner's reasoning is the assertion that Figure 1 of Pomerantz teaches a linker of 24 amino acids, corresponding to residues 41-65 of the GAL-4 dimerization element. In fact, Figure 1 of Pomerantz clearly and unambiguously shows that the domain used to dimerize two ZFGD1 molecules comprises all the amino acids of both the GAL-4 linker and dimerization element (Figure 1, bottom panel, Pomerantz):



Further, there is nothing in Pomerantz that teaches truncating the GAL-4 linker/dimerization element at amino acid residue 65. To the contrary, Pomerantz clearly teaches that their ZFGD1 dimers are formed by dimerization of the dimerization element extending from amino acids 41-100 and, moreover, that residues 66-100 are known to form part of the GAL-4 dimerization domain (Pomerantz, page 967, left column, emphasis added):

To test this model, we constructed the fusion protein ZFGD1, which contains fingers 1 and 2 of Zif268, a glycine residue, and residues 41 – 100 from GAL4 (Figure 1). Structural information is not available for residues 66 – 100 of GAL4, but these residues were included because they are known to form part of the GAL4 dimerization domain.

Thus, it is error to assert that Pomerantz teaches truncating the naturally occurring GAL4 domain at residue 65. In fact, the reference appears to label this residue solely because structural information on residues 66-100 was not readily available. However, despite the lack of structural information, Pomerantz clearly teaches that these residues are included in their molecules, making the total length of their dimerization domain is at least 59 amino acids in length, which clearly falls outside the scope of the pending claims.

The Examiner also errs in asserting that the binding sites of Pomerantz's ZFGD1-ZFGD1 dimers (or spacing between these binding sites) are relevant to the claimed subject matter. In this regard, the Examiner asserted (Examiner's Answer, paragraph bridging pages 6-7, emphasis in original):

Figure 1 is fully described by Pomerantz at e.g., page 967, col. 1, under the heading RESULTS. Pomerantz teaches that the chimeric protein is predicted to bind to a 25 base-pair site with the sequence 5'-CGCCAGAGGACAGTCCTCTGGGCG - 3'. The 6 base-pair zinc finger subsites (underlined) are present on each end of the extended site. The central 13 base pairs are **derived from a portion** of the GAL4-binding site that lies under the **coiled-coil dimerization motif** and associated peptide linker.

This description is utterly irrelevant to the claims on appeal – the GAL4 binding site that “lies under the coiled-coil dimerization motif” is entirely immaterial to the claims on appeal. This section of Pomerantz simply reiterates that the zinc finger domains (zinc finger 1 and 2 of each ZFGD1 molecule) bind to target sites of 3 base pairs each. Accordingly, one molecule of ZFGD1 binds to one of the underlined 6 base pair target sites. When two molecules are ZFGD1 are dimerized via the GAL4 dimerization domain (of at least 59 amino acids), the resulting ZFGD1-ZFGD1 homodimer was predicted to bind to the palindromic 6 base pair target sites separated by 13 base pairs. The central base pairs are not bound by the dimerization domain(s) and are not in any way germane to any of the claims on appeal.

In addition, it is error to assert that the background description in Pomerantz regarding “short” linkers in any discloses truncated the GAL4 dimerization domain from the fragment extending from 41 -100 Pomerantz deems necessary (Pomerantz, paragraph bridging pages 965-966 and first full paragraph of page 966, emphasis added):

Structure-based methods for linking DNA-binding modules provide another powerful design strategy (13). In this approach, computer modeling is used to superimpose protein – DNA complexes in various registers, revealing arrangements that might allow heterologous modules to be fused with short peptide linkers. ... Using this strategy...

Dimer formation, frequently employed by natural DNA-binding proteins to enhance the affinity and specificity of recognition, provides another attractive design strategy.

In other words, Pomerantz is disclosing their longer dimerization domains as an alternative to short peptide linkers.

Furthermore, the Examiner’s allegation on page 8 of the Examiner’s Answer that the coiled-coil region is known to be useful (based on references and the instant disclosure) is also not germane to the claims on appeal because these coiled-coiled domains are naturally occurring and/or longer than 30 amino acids and therefore are not encompassed by the pending claims.

Moreover, the Examiner’s assertion that Pomerantz somehow “suggests” truncating the GAL4 dimerization domain as claimed is completely factually erroneous.

In particular, in addition to the Examiner's assertions on pages 6-7 of the Examiner's Answer regarding Figure 1 (reproduced above), the Examiner also stated (Examiner's Answer, page 8):

Even assuming that Pomerantz teaches a 60-residue linker, as argued, however, Pomerantz employed this only to show the full sequence of GAL4 dimerization domain. Pomerantz teaches at e.g., page 967 col. 1, that structural information is not available for residues 66 – 100 which forms a part of the GAL4 dimerization domain. (It is also not apparent how the claim[ed] 30-residue linker without any description of its structure can link/fuse any zinc finger complexes).

The Examiner's assertion that Pomerantz concludes residues 66 – 100 are unnecessary (apparently because structural information was unknown) is completely outrageous. As repeatedly noted, Pomerantz didn't "employ" the entire dimerization domain only to show the full sequence – they used the entire dimerization domain because they believed residues 66 – 100 were critical to dimerization (Pomerantz, page 967, left column, emphasis added):

To test this model, we constructed the fusion protein ZFGD1, which contains fingers 1 and 2 of Zif268, a glycine residue, and residues 41 – 100 from GAL4 (Figure 1). Structural information is not available for residues 66 – 100 of GAL4, but these residues were included because they are known to form part of the GAL4 dimerization domain.

Therefore, it is clear that Pomerantz does not teach or suggest elements of the claims on appeal, including peptide linkers that are less than 30 amino acids in length.

Finally, it is error for the Examiner to raise new issues on appeal. *See*, parenthetical comment at the end of page 8 of the Examiner's answer, apparently attempting to question enablement.

Krylov does not cure the deficiencies of Pomerantz. The Examiner insistence that Krylov's coiled-coil heptads are 28 amino acids (4 heptads) long is in error. (Examiner's Answer, page 10). Indeed, as reiterated by the Examiner, Krylov clearly teaches that the

leucine zipper includes the amino acids shown on the top line of Figure 1B (labeled VBP). See, Figure 1B and corresponding legend of Krylov; page 2859, left column, first paragraph of Materials and Methods, emphasis in text added):

B

Peptad	1	2	3	4
VBP	I -T-T-I-R-A-P-L-E-K-E-I-N-T-A-L-E-T-E-V-Y-E-L-E-U-K-E	I -T-T-I-R-A-P-L-E-K-E-I-N-T-A-L-E-T-E-V-Y-E-L-E-U-K-E	I -T-T-I-R-A-P-L-E-K-E-I-N-T-A-L-E-T-E-V-Y-E-L-E-U-K-E	I -T-T-I-R-A-P-L-E-K-E-I-N-T-A-L-E-T-E-V-Y-E-L-E-U-K-E
coiled coil	g-a-b-e-d-e-f	g-a-b-e-d-e-f	g-a-b-e-d-e-f	g-a-b-e-d-e-f
R-E	R	R	R	R
R-K	R	R	K	R
R-K-J	R	R	R	K
R-K-J-J-K	R	R	R	R
Q-E-J-J-K	Q	Q	E	E

(B) the amino acid sequence of the leucine zipper region of VBP, the chicken version of the mammalian DBP, is presented using the single-letter code. Below the VBP sequence is the nomenclature for the positions in a coiled-coil. The sequence starts at the first ‘leucine’ position as defined previously (Vinson et al., 1989) and is grouped into heptads (**g,a,b,c,d,e,f**). ...

The sequence of the 96 amino acid host protein is ASM....**I**TIRAAFLE.... . The ‘leucine’ positions are in bold type.

Thus, by its own terms, Krylov states unequivocally that the leucine zipper region of VBP must include at least 3 amino acids N-terminal to the first heptads, namely the italicized “I” residue of Figure 1B that acts as ‘leucine’ before the first heptad and 2 amino acids flanking the last heptad. Thus, the leucine zipper domain of Krylov is 33 amino acids in length is excluded from the scope of all the claims. Moreover, the substitutions made to certain heptad residues are all within the context of the over 30 amino acid leucine zipper domain. As such, Krylov does not teach non-naturally occurring dimerizing leucine zipper domains.

For at least these reasons, neither Krylov nor Pomerantz teach or suggest peptide linkers of 30 or fewer amino acid residues as claimed. As the references do not disclose or suggest this claim element, there is no combination of Krylov and Pomerantz that

teaches all the elements of the claims and the rejection cannot be sustained on this basis alone.

b. A “derived” peptide as disclosed in Pomerantz is not non-naturally occurring

The references also fail to disclose non-naturally occurring peptide linkers of 30 or fewer amino acids in length. In response to Appellants’ previous arguments regarding Pomerantz’s failure to teach non-naturally occurring dimerization domains of any length and Krylov’s failure to teach non-naturally occurring leucine zipper domains of less than 30 amino acids, it was asserted (Examiner’s Answer, page 11, emphasis in original):

In reply, both the dimers of Pomerantz and Krylov are derived peptides. Each is a short length peptide which therefore lacks significant sequence identity with a naturally occurring peptide, as read in the light of the above-cited definition [of “derived”] in the specification. The art also defines non-naturally occurring as a recombinantly/synthetically made peptide or mutants as the one taught by Krylov. These mutants are therefore non-naturally occurring as they lack significant sequence identity with the natural leucine zipper peptide, consistent with the definition in the specification.

It is legal error on the part of the Examiner to read definitions of the specification into the references. It is also factually erroneous to assert that Pomerantz and Krylov’s dimerization domains “lack significant sequence identity” with naturally occurring peptides.

It is axiomatic that it is impermissible to read limitations from the specification into the claims. *See, e.g., E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted “in view of the specification” without importing limitations from the specification into the claims unnecessarily); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). Clearly then, it is impermissible to read definitions of a specification into a cited reference. Rather, the reference must be examined for what it teaches. In the case on appeal, Pomerantz teaches a naturally occurring GAL4 dimerization domain. Not only is

this naturally occurring GAL4 dimerization domain not a “short length peptide,” it also exhibits 100% sequence identity to the naturally occurring sequence – because it is the naturally occurring peptide. A non-naturally occurring peptide is one that does not occur in nature and Pomerantz’s GAL4 domain is clearly naturally occurring.

For its part, Krylov’s “mutants” are not 30 or fewer amino acids in length. In all cases, regardless of mutation, the leucine zipper region involved in dimerization includes not only the interacting heptads, but the surrounding amino acid residues (as shown in Figure 1B) of Krylov, bringing the length of Krylov’s “peptide” to 33 amino acids.

c. Pomerantz does not refer to Krylov to mutate and truncated GAL4 to join zinc finger modules

As acknowledged by the Examiner, Pomerantz’s reference to Krylov does not in any way mean that Pomerantz is suggesting that a truncated (heptad-only) leucine zipper domain could be used in place of GAL4 domains. *See*, Examiner’s Answer, pages 11-12:

In reply, Pomerantz [sic] reliance on Krylov is not based on substituting the coiled-coil linker Leu zipper of Krylov to the GAL-4 of Pomerantz. Rather, Pomerantz discloses that the coiled-coil region (a simple, well understood structure) of GAL4 can be similarly modified by mutation of the residues as taught by Krylov for the known, common coiled-coil structure as leu-zip. Each of the Pomerantz and Krylov references already teaches dimerization domains that are less than the claim undefined 30-residue length peptide. See rejections above.

Appellants fully agree that Pomerantz’s reference to Krylov is, at best, a suggestion that one or more of the 60 amino acids of the GAL4 dimerization domain could be modified in an analogous fashion to Krylov’s modification of one or more of the 33-amino acids of the VBP leucine zipper domain. *See*, page 970 of Pomerantz, which includes reference to Krylov (ref. 20), left column, emphasis added):

As demonstrated by many studies, the coiled-coil interaction motif offers the potential to modify the dimerization domain to increase dimerization affinity or to specifically promoter heterodimer formation (see refs. 19 and 20 for examples). Obligate heterodimer variants of the zinc-finger-GAL4 fusion might be constructed to ensure that the proteins could only bind to the heterodimer site. It also seems plausible that adjustments to the linker

region may give further improvements in the affinity and specificity of the zinc finger-GAL4 proteins.

However, it is completely untenable (and without a shred of supporting evidence) to assert that Pomerantz is suggesting both truncating and mutating the 60 amino acid GAL4 dimerization domain. To the contrary, as detailed on the record and above, Pomerantz unambiguously teaches that GAL4 should not be truncated because residues 66 – 100 are involved in dimerization.

It is also error to again assert that that Krylov teaches a peptide linker of 30 or fewer amino acids. As noted above, Krylov clearly and unequivocally teaches the leucine zipper region includes the 4 heptads and additional surrounding amino acids for a total of 33 amino acids. Indeed, Krylov repeatedly notes that the isoleucine (I) residue of the leucine zipper domain is a “leucine” position. *See*, Figure 1B of Krylov in which I is italicized indicating it is a leucine position and page 2859 left column, first paragraph Materials and Methods bolding this “I” residue and stating that “leucine” positions are shown in bold. Furthermore, Krylov teaches away from truncating the leucine zipper domain as it plainly states that at least 31 residues (including the “I” flanking the heptads) are required (and in their natural context) for dimerization.

d. Pomerantz does not refer to Krylov to use the leucine zipper domain to join zinc finger modules

Although the Examiner is adamant the obviousness rejection is not premised on the assertion that using Krylov’s leucine zipper domain instead of Pomerantz’s GAL4 domain is an obvious modification, Appellants nonetheless again address this issue inasmuch as this appears to have been the rejection stated by the Board in regards to the previously-appealed claims (*See*, Decision on Appeal mailed May 30, 2007, page 14):

Thus, the missing element from Pomerantz – non-naturally occurring peptide linkers, is supplied by Krylov. The skilled worker would have a reasonable expectation that Krylov’s domains could be utilized to complex zinc fingers to which they are attached in view of Krylov’s success in not only modifying their binding activity, but making it stronger (*i.e.*, more stable).

However, for the reasons of record, Krylov's modified leucine zipper domains, even if isolated from their natural context, must include residues flanking the 4 heptads (particularly the "I" that acts as part of the leucine zipper) and, therefore, is still greater than 30 amino acids in length and excluded from the scope of the claims on appeal.

In sum, neither Pomerantz nor Krylov teach or suggest a non-naturally occurring peptide linker of 30 amino acids or less, as claimed. Therefore, there is no combination of Pomerantz and Krylov that teaches all the claimed elements and, on this basis alone, the rejection cannot stand.

2. The obviousness rejection is also improper because truncating a mutated dimerization domain does not give predictable results

The obviousness rejection is also improper because the proposed modifications (truncations and mutations) to Pomerantz's GAL4 dimerization domains are not predictable from the teachings of the references and/or state of the art. Indeed, as the Supreme Court in *KSR v. Teleflex*, 550 U.S. 398, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007) reiterated, an obviousness inquiry is fact-dependent and that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 82 UPSQ2d at 1389. Instead, the combination of elements must result in a predictable outcome (see, Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in view of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. Vol. 72, No. 195, October 10, 2007, emphasis added):

The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one or ordinary skill in the art at the time of the invention.

It is also axiomatic that an obviousness rejection is improper where the proposed modification would destroy the intended function of the reference (see, e.g. *In re Fritch* 23 USPQ2d 1780, 1783, n.12 (Fed. Cir. 1992) and *In re Ratti* 123 USPQ 349, 352 (CCPA 1979)):

A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose.

[I]t would require a substantial reconstruction and redesign of the elements shown in [a cited reference] as well as a change in the basic principles under which [that reference's] construction was designed to operate.

In response to Appellants' previous arguments, it was asserted that truncation of GAL4 was not in any way unpredictable (Examiner's Answer, page 12):

There is nothing new, unobvious or unpredictable in varying the length of a known dimerization linker when its sequence is known and is varied in the context it is used. The prior art and specification (page 15, line 16) recognize the requirement for this linker to be of short length to be functional.

The Examiner's erroneous assertion that there is nothing unpredictable about "varying the length" (truncating) a known dimerization domain is not supported by evidence and completely contradicted by the references themselves. Indeed, it remains that case that there is no evidence whatsoever that Pomerantz's 60 amino acid GAL4 domain could be truncated and retain functionality. As noted repeatedly on the record and herein, Pomerantz clearly states that residues 66-100 are involved in dimerization and should be included. Thus, according to Pomerantz, removing these residues would destroy the intended function of their GAL4 dimerization domain.

Similarly, Krylov clearly states that the "I" residue flanking the heptads forms a part of the leucine zipper domain as it acts as 'leucine.' Thus, truncating Krylov's 33 amino acid dimerization domain to include only the 4 heptads (28 amino acids) is entirely unpredictable, and would destroy the intended function of the leucine zipper.

Thus, the references do not teach complexes comprising non-naturally occurring peptides 30 or fewer amino acids in length for joining zinc finger proteins. Moreover, the evidence of record establishes that it was completely unpredictable to take altered dimerization domains out of their natural context, shorten them to 30 amino acids or less and then use them in the context of zinc finger proteins.

For the reasons of record and as set forth above, the rejection to the claims on appeal cannot be sustained.

3. Separate argument regarding claim 21

For the reasons set forth in the record and above, Pomerantz and Krylov both fail to teach or suggest non-naturally occurring peptide linkers of 30 amino acids or less in length. In fact, both references teach that greater than 30 amino acids are required for dimerization. Thus, none of the claims on appeal can be obvious over the cited references.

Furthermore, Appellants note that claim 21 further requires that the peptide linker be between 5 and 25 amino acids in length. Even if Krylov did not teach away from truncating their 33 amino acid leucine zipper domain (which it does), and even if truncating this domain to only the heptads resulted in a functional dimerization domain (which it would likely not as it is missing one the residues involved in leucine zipper formation), such truncation would still result in a peptide of 28 amino acids, which is longer than the maximum length specified in appealed claim 21. Thus, claim 21 is separately patentable over the cited combination of references.

CONCLUSION

For the reasons stated above, Appellants respectfully submit that the pending claims are patentable.

Respectfully submitted,

Date: February 18, 2010

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CLAIMS APPENDIX

5. A zinc finger complex, comprising two or more fusion proteins, each fusion protein comprising a zinc finger protein that binds to DNA in a sequence-specific manner and a peptide linker, wherein the zinc finger proteins of the fusion proteins are joined to each other by specific binding of the peptide linkers, and wherein the peptide linkers are non-naturally occurring peptide linkers of 30 amino acids or less in length.

6. The zinc finger complex of claim 5, wherein the peptide linker of each fusion protein is the same.

20. The zinc finger complex of claim 5, wherein the zinc finger protein of each fusion protein has the same sequence.

21. The zinc finger complex of claim 5, wherein the peptide linker is between 8 and 25 amino acids in length.

EVIDENCE APPENDIX

No documents are attached to this appendix.

RELATED PROCEEDINGS APPENDIX

As noted above on page 2 of the previously-filed Appeal Brief, a Board Decision on Appeal in this case was mailed on May 30, 2007 and was attached to the Appeal Brief.